

DOCUMENT RESUME

ED 334 794

EC 300 540

AUTHOR Schopler, Eric
TITLE Neurobiological Correlates of Autism.
PUB DATE 11 Aug 90
NOTE 15p.; Paper presented at the Annual Convention of the American Psychological Association (Boston, MA, August 10-14, 1990).
PUB TYPE Information Analyses (070) -- Speeches/Conference Papers (150)
EDRS PRICE MF01/PC01 Plus Postage.
DESCRIPTORS *Autism; *Biological Influences; *Etiology; Genetics; Injuries; *Intervention; Neurological Impairments; *Neurology; Parent Influence; Perinatal Influences; Teaching Methods; Theories

ABSTRACT

This paper reviews the evidence for various biological mechanisms in autism and discusses implications of these mechanisms for treatment. A brief introductory discussion examines the history of research on autism. Then the literature is reviewed and treatment implications are drawn for the following biological mechanisms: genetic disorders; biochemical factors; birth injury; and structural abnormalities. The paper concludes that the evidence strongly supports the probability of multiple causation for the autism syndrome. Studies designed across diagnostic categories with a developmental perspective are encouraged. The limited clinical applicability of existing biological information is recognized, and practitioners are encouraged to continue to individualize intervention based on information about a particular child. The correction of the erroneous psychodynamic explanation basing autism on parental pathology is seen as the most important improvement in the treatment of autistic children. The effectiveness of structured instruction and the importance of teaching spontaneous communication are stressed. Includes 12 references. (DB)

* Reproductions supplied by EDRS are the best that can be made *
* from the original document. *

ED334794

U.S. DEPARTMENT OF EDUCATION
Office of Educational Research and Improvement
EDUCATIONAL RESOURCES INFORMATION
CENTER (ERIC)

☒ This document has been reproduced as
received from the person or organization
originating it.
☐ Minor changes have been made to improve
reproduction quality.

• Points of view or opinions stated in this docu-
ment do not necessarily represent official
OERI position or policy.

Neurobiological Correlates of Autism

Eric Schopler
Division TEACCH
University of North Carolina

APA Convention
August 11, 1990
Boston, Massachusetts

"PERMISSION TO REPRODUCE THIS
MATERIAL HAS BEEN GRANTED BY

Eric Schopler

BEST COPY AVAILABLE

EC 300540

It is difficult to discuss the biological basis of autism without first recognizing the historical context in which the syndrome first appeared. I will therefore start with a brief summary of that background, familiar to many of you, starting with Leo Kanner's introduction of autism into the mental health literature four decades ago. I will then review the evidence for some of the different biological mechanisms implicated in the autism syndrome, and what these may mean for our understanding. Since this symposium is under the auspices of Division 12, I will also discuss the implications of these biological mechanisms for treatment.

Background

When Kanner, in 1943, first published a series of 11 children for their similarities in diagnostic patterns, he included infantile autism. These children had difficulties with reciprocal relations from the beginning of life; their communication skills were impaired, reflecting a continuum of mental retardation, yet they had special interest and repetitive behaviors. Although Kanner hypothesized a constitutional predisposition for this syndrome, Freudian theory was riding high across every facet of problem considered childhood psychopathology at that time. Caught up in the ever present popularity of psychoanalytic theory, Kanner also tried to explain autism as a form of social withdrawal from unconscious hostility and rejection by well-to-do and highly educated parents; parents whose emotionally

controlled personalities and compulsive behavior produced high professional achievement and autistic children.

This explanation of autism led to counterproductive blame of parents, demoralizing their capacity to foster development in their own children. During the 1960's a perceptible shift occurred in the field of mental health, placing greater emphasis on the rules of evidence and empirical research than on the seductive metaphors of Freudian theory. In 1964 Rimland wrote a ground breaking review of the existing autism literature, convincingly showing the lack of evidence for psychogenesis and the greater likelihood of biological mechanisms producing the autism syndrome. Since that time the evidence for biologic basis for autism has been accumulating at an accelerating rate.

During the 1970's, a number of studies reported incidents of epilepsy among autism, which often occurred for the first time with onset of adolescence. Epilepsy occurs in 25 to 35% of the autistic population; at greater frequency with the more severely retarded population. When this frequency of seizures is compared with the incidence of 0.5 % among the general population, there can be little doubt that many cases of autism involve brain abnormality. In addition to the development of seizures, other biological mechanisms have been identified with varying amounts of supporting or replicating research evidence. No specific cause of autism has been discovered to date, but the

available evidence indicates that a number of different biological mechanisms can all produce the autism syndrome.

Biological Mechanisms

I will briefly review some of the major areas in which empirical data have been accumulating, identifying some neurobiologic processes involved with the autism syndrome. These include genetics, biochemical, birth injury, structural and metabolic factors.

Genetic disorders. That hereditary plays a significant role in a subgroup of autistic children was first demonstrated by the Rutter Folstein (1977) twin study in which the concordance rate for autism was 36% in the monozygote twins and) none in the dizygotic pairs. This concordance could not be explained by complications of pregnancy or by postnatal illness, and the finding supported the heritability autism. However, even more striking than the familial aggregation of autism, is the aggregation of related learning disorders in families of autistic children. 86% concordance rate was reported with related problems for monozygotic pairs in Rutter & Folstein (1977) study a much lower incidence of only 11% in dizygotic pairs.

In family studies, only a few multiple incidents of autism have been reported. Yet, with sufficient regularity to warrant an estimate of the occurrence in 2% of families with an autistic child. If this low occurrence is combined with the lowest prevalence figure for autism, 5 in 10,000,

then multiple incidence for autism occurs at 50 to 100 times what might be expected by chance.

Another source of genetic evidence is the recently discovered fragile X chromosome. This single gene disorder, found predominantly in males, appears to be associated with autism and other developmental disorders. Unusual features vary, but in the most severe form, the affected males tend to have elongated faces, low set ears, arched palate and enlarged testicles. Presence of fragile X can be assessed by blood tests including amino acid screen and karyotyping.

Treatment implications. The above evidence leaves little doubt that a small number of cases with autism and a larger number of related learning or social and cognitive difficulties, are associated with genetic transmission. This means that genetic counseling for parents or siblings may be indicated, except for cases in which autism is associated with a history of severe prenatal or postnatal trauma, or where there is no family history of autism or cognitive disabilities.

Biochemical factors. Evidence for abnormalities of neuroregulators in autism has been accumulating. Among the many neurotransmitters involved in the processing of behavior, serotonin has been of special interest. Already since the mid 1950's it was known that about 1/3 of individuals with autism, had elevated concentrations of blood serotonin, as did a significant number of others including the severely retarded. Scientific interest in

blood serotonin was further heightened when fenfluramine a drug previously used for weight control was used with 3 autistic children. Fenfluramine was known to lower serotonin levels, and when Ritvo and colleagues reported in the New England Journal of Medicine that a significant clinical improvement, including the doubling of IQ levels, had resulted from an open trial with the drug with only three children, a media inspired national interest in fenfluramine therapy was born. However, the resulting multiple studies did not replicate these dramatic findings. Instead they reported only a few children who showed improvement, similar to the occasional cure reported from case studies involving other specific therapies. Not only was the center study unable to replicate significant improvement, it also showed from spinal taps that serotonin levels decreased when either fenfluramine or placebo was dropped to baseline.

An interesting corrolary hypothesis was raised by Coleman. Since pyridoxine, a supplement used in Rimland's megavitamin therapy, is a co-enzyme involved with serotonin, and since a small percentage of autistic children have subnormal levels of serotonin, this subgroup should benefit from pyridoxine therapy, while those with high blood serotonin levels should receive fenfluramine therapy. Unfortunately, this intriguing proposal did not translate into a working therapy.

Dopamine has played a central role in current hypotheses about the action of antipsychotic drugs. It is based on the apparent clinical efficacy of dopamine receptor blockers which have been found effective in reducing hallucinations and thought disorders. This neurotransmitter hypotheses was tested with autistic children by Campbell with haloperidol. She reported that a subgroup of autistic children showed excessive dopaminergic activities, associated with stereotypies, hyperactivity and low intellectual functioning. Some long-term improvement has been reported for those subjects when tested with haloperidol. However, the negative side effect of tardive dyskinesia was also reported, though it was usually said to be reversible.

Another interesting biochemical hypothesis is the suggestion that abnormalities in the levels of endogenous opioids exists in some autistic children. These are involved in the regulation of pain, and it has been suggested that they may be involved in self mutilation. There have been some reports that the administration of naltrexone, an opiate antagonist, has resulted in the decrease of these symptoms. However, this effect has not been systematically demonstrated and replication is still being investigated.

In summary, it is fair to say that drug effects with autistic children have been based not so much on demonstration of neurotransmitter action, as on biochemical

processes not yet fully understood. Moreover, drug effectiveness has been sufficiently inconsistent with different autistic children, that drug therapy still has to be undertaken on an experimental basis with individual children. There is not yet any one preferred drug therapy for autism.

Birth Injury. It is difficult to identify risk factors specifically for autism before during, and after birth, as a wide variety of other neurological disorders have been found in association with autism. These include cerebral palsy, maternal rubella, tuberous sclerosis, meningitis, encephalitis and others. There are also studies showing that autistic children show excess of congenital minor, physical anomalies such as pathological reflexes, jerking, drooling, abnormal posture and gait, posturing of hands and fingers, tremor, emotional facial paralysis, and others. These often derive from prenatal and neonatal complications. In a recent review of the available evidence Luke Tsai (1987) identified a number of such unfavorable factors present more frequently in the history of autistic children than in comparison groups. These include older mothers, first and fourth or later born, bleeding after the first trimester, use of medication, and meconium in the amniotic fluid. Although not any one of these factors occurred more frequently with autistic children, when grouped together they had a higher frequency of unfavorable events than did their siblings. Although these pre, peri and neonatal

factors were found in only some of the autistic children, they do represent another source of evidence for the neurobiological basis of autism. While this information does not have direct implications for treatment, it does facilitate more accurate understanding and potential preventive measures

Structural abnormalities. The research for localized structural abnormalities of the brain in autism has been advanced by the development of high-tech methodology. Previous review of autopsy studies indicate abnormalities in left temporal lobe structure in a few autistic individuals. With the development of magnetic resonance imaging, enlargement in the fourth ventricle, accompanied by some cerebellar atrophy has been reported. However, this finding was not replicated by other investigators. On the other hand, Courchesne's MRI studies have revealed both structural and functional abnormalities of the cerebellum. However, it is not clear whether these are clinically significant. Autopsy (Bauman & Kemper) on two recent cases of autism revealed abnormalities in all areas of the hippocampus and related structures. These areas were characterized by reduced neuronal cell size and increased cell packing densely, Purkinje similar to developmentally immature structures. As with the abnormalities of the cerebellum, this represents only a very small sample.

The last possible subgroups of autism to be considered are those thought to be related to various metabolic

diseases. One example, is what Coleman referred to as purine autism. This designation was ascribed to a few cases of autism with evidence of an error in purine metabolism. These children had very high levels of uric acid excretion. Coleman acknowledges that uric acid levels have been known to vary with stress levels, and also the onset of adolescence. However, with various tests the purine processing disorder can be determined. A diet for purine autism or when ineffective, administration of allopurinol was said to appear effective in a few cases, but systematic study of this treatment has not yet been reported.

I have very briefly summarized the evidence for the biological bases of the autism syndrome, from research involving genetic, biochemical, structural and metabolic abnormalities. This material strongly supports the probability of multiple causation for the autism syndrome. Moreover, it bears keeping in mind that the three primary features defining autism involve rather diverse parts of brain anatomy. To complicate the issue of etiology further, behavioral functions of speech, social reciprocity, and special interests are developmentally determined, and do not appear at the same time. Hence research focused on specific sites with specific methods may not be able to unravel the biological mechanisms underlying autism. Instead studies designed across diagnostic categories, with a developmental perspective may offer the best hope for progress in understanding this disorder.

Likewise the clinical application of this growing fund of biological information is also very limited. Specific treatment techniques based on this research involving genetic counseling, drugs, megavitamins, or special diets has also been limited in their general application to autistic children, most of them have been shown effective with only a few autistic children, none have been effective with larger numbers of this population. Accordingly, optimum treatment still needs to be individualized according to the best information available for the particular child and relevant treatment options.

*(Example of Fenfuramine with heavy kids).

Probably the most important improvement in treatment of autistic children has resulted from the correction of the erroneous psychodynamic explanations basing autism in parental pathology with the recognition of the biologic mechanisms, even when specific mechanisms were not yet fully demonstrated, some important changes in treatment were possible.

Other improvements in treatment were based on the:

- 1) Parents were no longer regarded as the primary causal agent, but were seen as victims of the disorder much as the children themselves.

- 2) Thus history, information and observations of their own child could be accepted without reinterpretation, and the child could be helped through parental support and education.

3) Autism could be shifted from the emotional disorders to the developmental disorders, and effective educational intervention with the children could be developed.

4) It became clear through research, inspired in part by Marcel Kinsbourne, that these children learned better from structured than unstructured teaching situations.

5) That structured teaching could compensate some of the deficits involved with autism, such as problems with attention, memory, organization and auditory processing, difficulties with change and

6) That structured teaching could prevent many behavior problems, and increase children's functioning independently by developing physical structures clarifying confusion about where to be; schedules to help know when to be there, work/study systems showing amounts to be done and material organization showing how to do it.

7) Education could be organized around teaching spontaneous communication, regardless how limited the child's communication skill.

8) Social skills could be taught through peer models and in closer integration with the community. These improvements in the treatment have made an important difference in the lives of autistic people and their families. The clinical application of the more specific neurobiologic research is still in its earliest phases and will be realized in the future.

Bibliography for APA Talk by Eric Schopler
August 11, 1990
Title: Neurobiological Correlates of Autism

- Bauman, M. and Kemper, T.L. (1985). Histoanatomic observations of the brain in early infantile autism. Neurology, 35, 866-874.
- Campbell, M., Anderson, L.T., Cohen, K., Perry, R., Small, A.M., Green, W.H., Anderson, L., and McCandless, W. (1982). Haloperidol in autistic children: Effects on learning, behavior, and abnormal involuntary movements. Psychopharmacology Bulletin, 18 (1), 110-112.
- Coleman, M. and Gillberg C. (1985). The biology of the autistic syndromes. New York: Praeger Publishing.
- Courchesne, E. (1988). Neuroanatomical sustems involved in infantile autism: The implications of cerebellar abnormalities. In G. Dawsons (Ed.), Autism: New perspectives on diagnosis, nature, and treatment. (pp.119-143). New York: Guilford Publishing Company.
- Folstein, S. and Rutter, M. (1977). Infantile autism: A genetic study of twin pairs. Journal of Child Psychology and Psychiatry, 18, 297-321.
- Geller, E. Ritvo, E.R., Freeman, B.J., and Yuwiler, A. (1982). Preliminary observations on the effect of fenfluramine on blood serotonin and symptoms in three autistic boys. New England Journal of Medicine, 307, 165-169.
- Kanner, L. (1943). Autistic disturbances of affective contact. Nervous Child, 2, 217-250.
- Panksepp, J. and Sakley, T.L. (1987). Possible brain opioid involvement in disrupted social intent and language development of autism. In E. Schopler and G. Mesibov, (Eds.), Neurological Issues in Autism (pp. 357-368). New York: Plenum Press.
- Rimland, B. (1964). Infantile autism. New York: Appleton-Century-Crofts.
- Rutter, M.. (1970). Autistic children: Infancy to adulthood. Seminars in Psychiatry, 2, 435-450.

Schopler, E., Brehm, S.S., Kinsbourne, M., and Reichler, R.J. (1971) Effect of structure on development of autistic children. Archives of General Psychiatry, 24, 415-421.

Tsai, L. (1987). Pre-, peri-, and neonatal factors in autistics. In E. Schopler and G. Mesibov, (Eds.) Neurological Issues in Autism. New York: Plenum Press.